Ref. 1

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Memorandum

Date March 23, 1998

From Division of Product Manufacture and Use, HFS-246
Chemistry Review Team

Subject **CAP 7C0208** (MATS M2.3): Cosmetic, Toiletry, and Fragrance Association (CTFA), submission of 18 December, 1997. Petition for the safe use of carbon black in cosmetics (including eye area use).

To Division of Petition Control, HFS-215
Attn.: Richard White

1. Introduction

The Cosmetic, Toiletry, and Fragrance Association (CTFA) has submitted a petition to amend 21 CFR Part 74, *Color Additives Subject to Batch Certification*, to provide for the safe use of high purity furnace black (HPFB) for use in cosmetics, including eye area use. In this newest submission, CTFA responds to a series of questions asked by the agency in a letter to CTFA of 3 Dec. 1992.[1] Specifically, the submission confirms the identity of the additive, provides updated specifications for HPFB, and presents a lifetime cancer risk assessment for the polyaromatic hydrocarbon (PAH) contaminants in HPFB. CTFA has retained their previously presented exposure estimate to carbon blacks from the petitioned uses.

CRT evaluated exposure and related issues in a previous memorandum.[2] In that memorandum, CRT derived an exposure estimate to the color additive and to polyaromatic hydrocarbons (PAH) contaminants based on the requested uses.

2. Identity of the Additive

CTFA clarifies that the petition is now only intended to cover the use of high purity carbon black made by the furnace process (high purity furnace black, HPFB); it will no longer include other carbon black products (specifically, carbon black manufactured by the channel process). HPFB was also the subject of FAP 5B4464, from the Cabot Corporation, and the information from that petition is incorporated by reference into the current document. That petition resulted in an amendment to §178.3297, *Colorant for polymers* to provide for the safe use of the color additive in polymers intended for use in contact with food.[3]

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[1] See letter from W. Long, FDA to G. N. McEwen, CTFA, 3 Dec., 1992.

[2] Memorandum from G. Cramer, HFF-415, to M. Kashtok, HFF-334, of 25 July, 1990.

[3] 62 FR 25475, 9 May, 1997

1987C-0023

High purity furnace black (HPFB) is essentially pure carbon, formed as aggregated particles. The commercial product is manufactured by the combustion of aromatic hydrocarbon fuels. Table 1, below, summarizes some characteristics of the additive.

Table 1: Identity of the Additive

1. Chemical name:	carbon black, furnace process
2. Common and trade names:	High purity furnace black (HPFB), CI Pigment Black, gas black; Black Pearls (Cabot) [many trade names]
3. CAS Registry Number:	1333-86-4 (for all carbon blacks); CI 77266
4. Structure:	aggregates of roughly spherical particles in chains or spheres consisting of carbon
5. Appearance:	black powder or pellets
6. Composition	> 98% Carbon (C)

3. Contaminants in Carbon Black

An important consideration in evaluating the use of carbon black is the presence of polyaromatic hydrocarbon (PAH) contaminants. Analytical data have shown that 22 different PAHs may be present at various levels in carbon black pigments, including benzo[a]pyrene (B[a]P), a known carcinogen. High purity furnace blacks are generally distinguished from other carbon blacks by having less than 5 ppm of 12 principal extractable PAHs,[4] and less than 2 ppb of benzo[a]pyrene.[5]

Another important characteristic distinguishing HPFB from other carbon black products is the surface area of the material, which is inversely related to the particle size. Larger surface area, corresponding to smaller particle size, is proportional to its affinity for PAHs. Carbon blacks with larger surface areas (ie, smaller particle sizes) have notably lower extractable-PAH fractions.[6] Because particle sizes (and surface area) vary widely depending on the manufacturing

[4] Fluoranthene, pyrene, cyclopenta[cd]pyrene, chrysene, benz[a]anthracene, benzo[e]pyrene, benzo[a]pyrene, benzo[ghi]perylene, indeno(1,2,3-cd)pyrene, dibenzo[ah]anthracene, anthanthrene, and coronene (p. 000006).

[5] FAP 7C0208, vol. I, p. 000006

[6] See for example, abstracts from Falk, H. L. and Stein, P. E. Cancer Research **12**:30-39, 40-43 (1952); Hase, A., Lin, P. H. and Hites, R.A., Carcinogenesis--Comprehensive Survey **1**:435-442 (1976); Lakowicz, J. R., and Bevan, D. R., Biochemistry **18**(23):5170-5176 (1979); Pylev, L. N., and Yenkova, G. D., Gigienda Truda I Professional/nye Zabolevaniya **17**(4):52-52 (1974). It is not well-known whether the lower amount of extractables is strictly due to tighter binding between PAHs and carbon blacks, or due to higher capacity.

process and conditions, HPFB will carry a surface area specification that is, in part, intended to limit extractable-PAH contamination.

CTFA has proposed the following contaminant specifications for their HPFB products (Table 1 of Appendix to this submission):

Table 2: Contaminant Specifications

Contaminant	Limit
As	≤ 3 ppm
Pb	≤ 10 ppm
Hg (total)	≤ 1 (ppm)[7]
Total sulfur	≤ 0.5%
Toluene extractable sulfur, as benzothiophene derivatives	≤ 0.1 ppm
Total PAHs	≤ 0.5 ppm
Benzo[a]pyrene	≤ 0.005 ppm (5 ppb)
Benzo[a,h]anthracene	≤ 0.005 ppm (5 ppb)

The petitioners state that the analytical methodology for the detection of specific PAHs allows for the detection of 22 different species with a sensitivity of 1 ppb, each.

The agency has previously commented on appropriate specifications for carbon blacks for food-contact use (FAP 5B4464). In regulating this color additive for polymers for food contact uses the agency decided that "specifications are necessary to ensure that the risk from PAH's resulting from the proposed use of high-purity furnace black in food-contact applications is insignificant and that use of the additive is safe. Therefore, the regulations set forth in this document prescribe that high-purity furnace black shall not contain total PAH's in excess of 0.5 parts per million and shall not contain benzo[a]pyrene in excess of 5.0 ppb."[8] Because these specifications were deemed necessary for an indirect additive use of HPFB, we conclude that maintaining individual specifications for these contaminants in cosmetic formulations is also appropriate. Since dibenzo[a,h]pyrene is at least as carcinogenic as benzo[a]pyrene, maintaining a specification for this contaminant is appropriate as well (see section 5).

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[7] Although the units were left off the limit for mercury, we assume that the limit is 1 ppm.

[8] 62 FR 25475 at 25476.

4. Exposure Estimate to HPFB

Although the petition requests listing HPFB for use in cosmetics generally, CTFA listed the following major uses for carbon black in cosmetic formulations: eyeliner, brush-on-brow, eye shadow, mascara, lipstick, blushes and rouge, makeup and foundation, and nail enamel. Uses of these products cover three principal routes of administration for exposure: dermal, ocular, and oral. The new submission states that the petition now covers only the use of HPFB for use in cosmetic products, but retains CTFA's earlier exposure estimate. Therefore, HPFB would substitute for other grades of carbon blacks in these products.

The exposure estimate provided by CTFA (pp. 000339-340) was broken down by product category as described below. This list has not changed from the original submission, and is presented in Table 3 for ease of reference.

Table 3: CTFA's Exposure Estimate to HPFB from Cosmetic Products

Product	Color Conc.	Use Level of product (mg/p/d)	Color exposure (mg/p/d)	Exposure (mg/kg-bw/d)*
Ingested Cosmetics				
lipstick	1%	73	**0.73**	**0.002**
Eye area use cosmetics				
eyeliner	30 %	9.9	2.97	
brush-on-brow	30 %	5.5	1.65	
eye shadow	30 %	7.9	2.37	
mascara	10 %	24.7	2.47	
			9.46	**0.19**
Other externally applied cosmetics				
blushes and rouge	2 %	13.6	0.272	
makeup, foundation	5 %	265.0	13.25	
nail enamel	2 %	56.0	1.12	
			14.40	**0.29**

*Assuming a 50-kg body weight.

Assuming that eye-area cosmetics would be applied three times per day, and using an average body weight of 50 kg, CTFA arrived at an overall exposure to HPFB from the above products of approximately 0.87 mg/kg-bw/d (corresponding to 44 mg/p/d). They claimed that additional exposure from possible carbon black used in soaps, temporary hair color rinses, creams, or lotions were not expected to raise the total exposure over 1 mg/kg (corresponding to 50 mg/p/d exposure). In the new submission, CTFA repeated their exposure estimate, although they did not provide any information about carbon black uses in soaps, temporary hair color rinses, creams, or lotions.

CRT (formerly FCARS) previously calculated an exposure estimate for carbon black to be used in these products (ref. 2). This exposure estimate was developed using product use information from the cosmetic industry and color exposure scenarios developed by the Hart Panel.[9] Our earlier estimates were calculated for individuals using the 90th percentile amount of each cosmetic product per day. These quantities were calculated by multiplying the 90th percentile frequency of use by the average amount of a cosmetic product used per application.[10] That exposure estimate also allowed for the fraction of the color additive expected to be available for absorption (rather than assuming all of the color additive in the product would be absorbed), but assumed that all available color is absorbed. We will retain these principles. The FDA exposure estimate is shown below:

Table 4: FDA Exposure Estimate for HPFB from Cosmetic Products

Cosmetic Product	mg product used/day	Color conc.	Color used per day (mg)	% Color avail for absorption	Color exposure (mg/p/d)
Ingested cosmetics					
lipstick	20	1 %	0.2	50	0.1
Eye area use cosmetics					
eyeliner	10	30 %	3.0	50	1.5
brush-on-brow	5.5	30 %	1.6	50	0.8
eye shadow	7.9	30 %	2.4	50	1.2
mascara	25	10 %	2.5	50	1.2
Other externally applied cosmetics					
blushes and rouge	14	2 %	0.3	50	0.2
makeup and foundation	265	5 %	13	50	6.5
nail enamel	56	2 %	1.1	0	0

[9] Hart, et al., Risk Anal. 6(2) 117-154 (1986)

[10] See for example, CMF 9, submission of 29 June, 1983.

As noted in the 25 June, 1990 memorandum, it is unlikely that any individual will be a 90th percentile consumer of all of the above cosmetic products. Therefore, total exposure from external cosmetic should not be estimated by adding the 90th percentile exposures. Total exposure to HPFB, however, likely falls between 1 and 10 mg/p/d. Because we normally assume an average body weight is 60 kg (rather than 50 kg), this exposure is equivalent to 0.017 to 0.17 mg/kg-bw/d. As noted above, no information was provided regarding the use of carbon blacks in soaps, hair rinses, creams, or lotions. Although CTFA has requested use in cosmetic products generally, we believe that the conservatism underlying our exposure estimate will cover the unspecified uses in lotions, hair rinses, creams, and lotions.

5. Risk Assessment for PAHs from HPFB

Section C of this submission (p. 7) presents the risk assessment performed by CTFA for exposure to the polyaromatic hydrocarbons associated with carbon black. The risk assessment uses a toxic equivalency factor (TEF)-based method to estimate exposure from the carcinogenic PAHs. TEFs are factors that scale the relative carcinogenicity of each substance in relation to a selected standard. Here, the toxicities of the PAHs are scaled compared with that of benzo[a]pyrene. TEFs for the various PAHS are presented in Table 2 of the submission. Based on the TEF values presented in the submission, benzo[a]pyrene and dibenzo[a,h]pyrene have the highest toxicity. Five PAHs account for the bulk of the toxicity associated with this class of molecules:

Table 5: Carcinogenic PAHs and their TEFs

PAH	TEF
Dibenzo[a,h]pyrene*	1.05
Benzo[a]pyrene	1.0
Anthanthrene	0.32
Naphthalene	0.28
Indeno[1,2,3-cd]pyrene	0.25
*listed as benzo[a,h]pyrene in the specifications	

The TEFs for all the other PAHs are lower, ranging from 0.001 to 0.1.

To obtain the total toxicity associated with all of the PAHs in a sample, the concentration of each PAH species is multiplied by its TEF.[11] For this risk assessment, CTFA used the

[11] TEFs, toxic equivalency factors, are factors that weight the relative toxicity of a species, in this case, the various PAHs, to a specific compound, here, benzo[a]pyrene. Thus, the TEF for B[a]P is unity, and the TEF for a PAH with lower toxicity is less than 1. TEF's for PAHs are reported by I. C. T. Nesbit and P. K. LaBoy, Reg. Tox.

concentrations from the grade of carbon black that had the highest total PAH content. (It was unclear, however, whether the grade of HPFB used for the risk assessment meets the specifications for the petitioned color additive.) The products of the concentrations and TEFs for all 22 species were then summed to yield the B[a]P-equivalent concentration.[12] According to the petition, this method resulted in a total toxicity-weighted PAH content of 43 ppb B[a]P-equivalent for the sample they analyzed.

CTFA used the worst-case assumption that all of the PAHs present in the carbon black used in cosmetic formulations migrate into the body. They then used the B[a]P-weighted PAH exposure to compute the lifetime cancer risk due to these compounds. Using their exposure estimate to the color additive of 50 mg/p/d and a B[a]P-equivalent PAH concentration of 43 ppb, CTFA calculated an exposure of 4.3×10^{-8} mg PAH as B[a]P/kg-bw/d (2.12 ng PAH as B[a]P/p/d). (See pp. 8-9 of the submission.) Multiplying this exposure by the (FDA-derived) unit risk factor[13] for B[a]P of 1.75 $(\text{mg/kg-bw/d})^{-1}$ resulted in a lifetime cancer risk of 4.3×10^{-8}.

Using a TEF-based approach is acceptable, and has precedent (see for example, EPA risk assessment for dioxins,[14,15] or FDA risk assessment for consumption of fish after the Exxon Valdez oil spill). To evaluate CTFA's analysis of the B[a]P-equivalent contamination in a sample of HPFB, we performed a similar calculation, but assumed that benzo[a]pyrene and benzo[a,h]anthracene were both present at 0.005 ppm, the proposed limit. We then assumed that each of the 20 other PAHs would be present in equal amounts, with a total PAH concentration of 0.5 ppm. This resulted in a concentration of 0.0245 ppm for each other PAH.[16] Multiplying these concentrations by the TEFs and summing the products resulted in a total B[a]P-weighted concentration of 44 ppb. This value is essentially the same as that presented by CTFA.

We disagree, however, with CTFA's risk assessment because we believe it to be too

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[12] That is, the toxicity of the contaminants as if they were all benzo[a]pyrene.

[13] QRAC memorandum of August 9, 1990.

[14] CTFA cites a precedent for this type of analysis, specifically, the 9 August, 1990 Report from the Quantitative Risk Assessment Committee on the "Estimation of Risk Associated with Consumption of Oil-contaminated Fish and Shellfish by Alaskan Subsistence Fishermen Using a Benzo[a]pyrene Equivalency Approach."

[15] NATO Report No. 178, " Scientific Basis for the Development of the International Toxicity Equivalency Factor (I-TEF) Method of Risk Assessment for Complex Mixtures of Dioxins and Related Compounds" (Dec. 1988)

[16] Calculation: $C = \{0.5 - 2(0.005)\}/20$, where 0.5 is the total concentration of all 22 PAHs (ppm), 0.005 is the concentration limit for benzo[a]pyrene and benzo[a,h]anthracene, "2" accounts for the fact that there are two species whose concentrations are independently limited to this amount (0.005 ppm), and 20 is the number of other PAHs whose concentration is to be determined.

conservative in estimating (a) the exposure to HPFB (and thence to the contaminants) and (b) the amount of PAH that would be available for absorption into the body from HPFB. For our calculation, we will use the exposure we calculated above as a starting point. Combining the color additive exposure of 10 mg/p/d (0.17 mg/kg-bw/d), with the PAH concentration results in a B[a]P-equivalent PAH exposure of 0.43 ng/p/d (4.3 x 10^{-7} mg/p/d, 7.2 x 10^{-9} mg PAH/kg-bw/d).[17]

Although CTFA assumed that all the PAHs were available for absorption into the body, we believe that this assumption is too conservative, as well. As the petitioners noted, typical extractions of PAHs require severe conditions, such as Soxhlet extraction with solvents such as dichloromethane, for up to 150 hours. In fact, the petitioners state that they expect the available PAH concentration to be at most 0.005% of the total toluene-extractable PAHs. They support this argument by citing the severe conditions necessary to extract PAHs from carbon black, and the stronger affinity of carbon black for PAHs compared with either vehicles used in cosmetic formulations or human and animal sera.[18] The current submission contains additional data addressing the issue of bioavailability of PAHs from carbon black manufactured by the furnace process, including the affinity of the product for polyaromatic hydrocarbons (PAHs) (see section B.1, p. 6). In further support of this argument, we note that activated charcoal, having a similar structure and composition to carbon black, is used expressly to remove impurities such as PAHs or other organic compounds by adsorption.

The amount of PAHs available for absorption from carbon blacks would be much lower than the toluene-extractable concentration. In our 7/25/90 memorandum, the fraction available for absorption was assumed to be 10%. We will retain this factor, noting that PAH availability is likely much lower than this. If we assume that 10% of the total PAHs can be absorbed into the body from the carbon black, we obtain an exposure to the B[a]P-equivalent PAHs of 4.3 x 10^{-8} mg/p/d (7.2 x 10^{-10} mg/kg-bw/d). Applying the unit risk factor for B[a]P, we obtain a lifetime cancer risk of 1.25 x 10^{-9}.

As a component of their risk analysis, CTFA made a comparison of the B[a]P-equivalent concentration of 43 ppb to the 0.5 ppm (500 ppb) regulatory limit proposed for PAHs, arguing that because 43 is less than 500, CTFA's proposed use is safe. We disagree with CTFA'S comparison of the B[a]P-equivalent concentration to the limit on PAHs. CTFA failed to note that the weighted concentration computes the toxicity of the PAHs as if only B[a]P were present, while the 0.5 ppm total PAH limit refers to the array of PAHs with their different TEFs. Comparing an analytical value obtained directly from a physical measurement (such as the

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[17] Calculations: 10 mg/p/d * 43 ppb = 4.3 x 10^{-10} g/p/d÷ 60 kg = 7.2 x 10^{-12} g/kg-bw/d.

[18] See for example, Bevan, D. R. and Worrel, W. J. (1984) "The Bioavailability of Benzo(a)pyrene Adsorbed to Carbon Black" in: Polynuclear Aromatic Hydrocarbons: Mechanisms, Methods, and Metabolism, 8th Intl. Symposium, Cooke, M. and Dennis, A. J., eds., Batelle Press, or Lakowics, J. R. and Bevan, D. R. (1980) "Transport of a Carcinogen, Benzo[a]pyrene, from Particles to Lipid Bilayers," Biochim. Biophys. Acta **629**:243-258.

concentration of a single PAH species) to a weighted concentration that cannot be obtained directly by analytical means is inappropriate. This assumption was therefore not used in our risk assessment rationale.

6. Conclusions

CTFA has limited the scope of this petition to request only the use of high purity furnace black (HPFB) as a color additive for use in cosmetic products. Based on the types of products and use levels cited in the petition, we have estimated that the exposure to HPFB would not exceed 10 mg/p/d (0.17 mg/kg-bw/d). A risk assessment using a TEF approach was used by CTFA to calculate the combined lifetime carcinogenic risk from exposure to all PAHs in a sample of HPFB, on a benzo[a]pyrene basis (B[a]P). The B[a]P-equivalent concentration of PAHs was 43 ppb. Using the FDA's unit risk value for B[a]P, we calculated that the lifetime cancer risk associated with the PAHs in carbon black would be no greater than 1.25×10^{-9}. The Quantitative Risk Assessment Committee should be asked to verify this risk calculation.

We have no further questions regarding this petition.

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HFS-226; HFS-245; HFS-248

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